American Journal of Hematology 62:129–138 (1999)

The Perioperative Complication Rate of Orthopedic Surgery in Sickle Cell Disease: Report of the National Sickle Cell Surgery Study Group

Elliott P. Vichinsky,[1]* Lynne D. Neumayr,[1] Charles Haberkern,[2] Ann N. Earles,[1] James Eckman,[3] Mabel Koshy,[4] and Dennis M. Black[5]

[1]Department of Hematology/Oncology, Children's Hospital Oakland, Oakland, California
[2]Children's Hospital and Medical Center, Seattle, Washington
[3]Emory University School of Medicine, Atlanta, Gerogia
[4]University of Illinois, Chicago, Illinois
[5]Prevention Sciences Group, University of California, San Francisco, California

Orthopedic disease affects the majority of sickle cell anemia patients of which aseptic necrosis of the hip is the most common, occurring in up to 50% of patients. We conducted a multicentered study to determine the perioperative complications among sickle cell patients assigned to different transfusion regimens prior to orthopedic procedures: 118 patients underwent 138 surgeries. The overall serious complication rate was 67%. The most common of these were excessive intraoperative blood loss, defined as in excess of 10% of blood volume. The next most common complication was sickle cell-related events (acute chest syndrome or vaso-occlusive crisis), which occurred in 17% of cases. While preoperative transfusion group assignment did not predict overall complication rates, higher risk procedures were associated with significantly higher rates of overall complications. Transfusion complications were experienced by 12% of the patients. Two patients died following surgery. Both deaths were associated with an acute pulmonary event. The 52 patients undergoing hip replacements experienced the highest rate of complications with excessive intraoperative blood loss occurring in the majority of patients. Sickle cell-related events occurred in 19% of patients, and surgical complications occurred after 15% of hip replacements and included postoperative hemorrhage, dislocated prosthesis, wound abscess, and rupture of the femoral prosthesis. There were twenty-two hip coring procedures. Acute chest syndrome occurred in 14% of the patients. Overall, decompression coring was a safer, shorter operation. A randomized prospective trial to determine the perioperative and long-term efficacy of core decompression for avascular necrosis of the hip in sickle cell disease is needed. In conclusion, this study demonstrates a high rate of perioperative complications despite compliance with sickle cell perioperative care guidelines. Pulmonary complications and transfusion reactions were common. This study supports the results previously published by the National Preoperative Transfusion in Sickle Cell Disease Group. These results stated that a conservative preoperative transfusion regimen to bring hemoglobin concentration to between 9 and 11 g/dl was as effective as an aggressive transfusion regimen in which the hemoglobin S level was lowered to 30%. Am. J. Hematol. 62:129–138, 1999.

Key words: sickle cell disease; surgery; orthopedics; transfusion

INTRODUCTION

Orthopedic disease affects the majority of sickle cell anemia patients, and as their life span increases, most patients will undergo at least one orthopedic surgical procedure. Specifically, surgical treatments of bone infection, correction of muscular skeletal deformities, and hip surgery are now very common. Bone infections affect

Contract grant sponsor: Northern California Comprehensive Sickle Cell Center of the Sickle Cell Disease Branch of the National Heart, Lung and Blood Institute; Contract grant number: HL-20985.

*Correspondence to: Elliott Vichinsky, MD, Children's Hospital Oakland, 747 52nd Street, Oakland, CA 94609. E-mail: evichinsky@lanminds.com

Received for publication 22 October 1998; Accepted 4 August 1999

almost 10% of patients and are usually surgically treated [1]. Orthopedic surgery to alleviate muscular skeletal deformity is increasingly performed among the 20% of patients who have experienced a neurologic event [2]. Aseptic necrosis of the hips is the most common orthopedic complication, occurring in up to 50% of patients [3–6]. Most cases are now surgically treated either with decompression coring procedure in early stages or with hip replacement in advanced stages.

As orthopedic surgery becomes more common in patients with sickle cell anemia, understanding the perioperative morbidity of these interventions is essential. Previous reports found complication rates ranging from less than 5% to over 50% after a variety of surgical procedures in this patient population [7–13]. However, these studies were largely retrospective and included limited numbers of patients. Standardized perioperative treatment and monitoring plans were not utilized, and patient risk factors were not identified.

A multi-center sickle cell surgery study group was initiated in 1988 to address the question of perioperative treatment and outcome of patients. The aims of the study group were (1) to develop a standardized, multidisciplinary, perioperative treatment plan; (2) to compare the rates of perioperative complications among patients assigned to different preoperative transfusion regimens, including aggressive and conservative preoperative transfusion; (3) to determine the risk of specific surgical procedures; and (4) to identify factors that predict complications.

This multi-center Preoperative Transfusion Study in Sickle Cell Anemia included 138 orthopedic procedures. In this report, we describe the patient characteristics, perioperative management, and complication rates associated with these procedures. Two-thirds of the orthopedic procedures in this study involved the hip and, therefore, constitute the largest group of hip surgeries reported in sickle cell disease. As a result, we are able to compare the perioperative outcome of joint replacement with that of core decompression for avascular necrosis of the hip.

MATERIALS AND METHODS

Patients were enrolled from 26 centers. Each institution had a principal investigator, data coordinator, anesthesiologist, nurse, and surgeon assigned to the study. As previously described, a protocol was followed, and extensive data were collected from the time of registration through a 30-day postoperative period [14]. Institutions were randomly site-visited for verification of patient records and compliance with perioperative management guidelines.

Patient Eligibility

Patients with sickle cell anemia or sickle β-thalassemia^0 who were undergoing elective surgery (defined as patients not requiring emergency surgery within 12 h of registration) were eligible for study entry. After informed consent was obtained, individuals were randomized to group one, aggressive transfusion to decrease the hemoglobin S level to less than 30% and to increase hemoglobin concentration to 10 g/dl (range, 9–11), or group two, simple transfusion to increase hemoglobin level to 10 g/dl (range, 9–11) only. The method of transfusion in group one (rapid partial exchange, subacute partial exchange, and simple transfusions) was left to the discretion of the investigator [14]. Patients who had more than one operation were randomly reassigned to a transfusion group for each subsequent procedure. In order to track the natural history of surgical interventions in sickle cell disease, data were prospectively collected on all surgical cases at the participating centers. If patients declined randomization or had been transfused within 3 months of their surgical date, they were eligible for registration in one of two additional groups: group three consisted of patients not transfused in the preoperative period, primarily due to the discretion of the principal investigator; group four consisted of patients who were transfused but not randomized. Standardized perioperative management guidelines and data collection were the same for all four groups.

From August of 1988 through August of 1993, 153 patients were enrolled in the study. Fifteen surgeries were subsequently canceled. A total of 118 patients underwent 138 procedures; 74 of these procedures were randomized to group one or two, and the remainder were registered in the nonrandomized groups.

Perioperative Management and Data Collection

Detailed perioperative treatment and transfusion protocols have been previously described [14]. The patients' medical and surgical histories were recorded, and the anesthetic risk, i.e., American Society of Anesthesiologists physical status [15], was determined. Extensive baseline testing included room-air oxygen saturation and chest roentgenograms. Additionally, all patients had serial hemoglobin, hemoglobin S %, renal function, liver function, and oxygen saturation studies. All patients received sickle-negative blood, and, if there was a history of febrile transfusion reactions, they received leucocyte-reduced blood. Leukocyte reduction was accomplished either through washing or filtration. The presence of alloantibodies was determined with standard screening techniques [16]. Each operation was classified as low risk (e.g., bunionectomy or hip coring) or intermediate risk (e.g., hip replacement or spinal surgery) according to an established risk classification for surgical procedures [14].

All complications occurring from study entry through the 30-day postoperative period were recorded as minor (minor wound infections and brief temperature elevations lasting less than 48 h and not exceeding 38.5°C),

serious (complications causing prolonged hospitalization), or life-threatening. Detailed, standardized data forms were completed for the specific complications including acute chest syndrome, vaso-occlusive crisis, neurologic dysfunction, renal dysfunction, serious infection with fever, and alloimmunization. Acute chest syndrome was defined as a new pulmonary infiltrate involving at least one full segment of the lung; atelectasis was excluded from this definition. Vaso-occlusive crisis was defined as nonsurgical pain lasting longer than 24 h and requiring opioid analgesia. Specifically, only pain for which there was no other explanation and was described by the patient as typical for their crisis was considered vaso-occlusive crisis. Acute chest syndrome and vaso-occlusive crisis were considered "sickle cell-related events." Fever or infection was defined as a temperature higher than 38.5°C or a documented infection lasting at least 48 h (and not attributed to acute chest syndrome). Intraoperative complications were also specifically defined and included hypo-/hypertension, hypo-/hyperthermia, hypoxia, and acidosis. Intraoperative blood loss exceeding 10% of blood volume was defined as excessive in this severely anemic population. All antibodies were checked against the patient's blood-banking records, and alloimmunization was defined as a new, clinically important red-cell antigen.

STATISTICAL ANALYSIS

Means are reported ± one standard deviation. Demographic and laboratory data were compared across the transfusion groups using the continuity-corrected chi-square analysis or the Fisher exact test for categorical data, and ANOVA for comparisons of continuous variables. Kruskal–Wallis or Wilcoxon two-sample tests were utilized when comparing continuous variables that were not normally distributed.

Continuity-corrected chi-square analysis was used to identify possible risk factors from patient demographic data, past medical history, and laboratory values, and the surgical risk score for the development of any serious complication and for the development of a sickle cell-related event with orthopedic surgery in sickle cell anemia. Nonparametric tests were utilized to identify possible risk factors for intraoperative blood loss associated with hip replacement surgery.

As some patients had more than one surgical procedure in the study, all tables and statistical comparisons summarize surgical cases, not necessarily unique patients. However, the analysis was repeated after eliminating second procedures in the same patients, reducing the total sample size to 118, and any significant findings are noted in the Results section.

TABLE I. Distribution of Orthopedic Surgeries

Surgical procedure	Total group ($N = 138$)*	% of Total
Hip replacement	52	38%
Hip coring	22	16%
Other hip surgery	20	14%
Tendon lengthening	11	8%
Debridement	10	7%
Miscellaneous	23	17%
Surgical Risk		
Risk 1	80	58%
Risk 2	58	42%

*The group number refers to the total number of operations.

RESULTS

All Orthopedic Procedures

Surgical subtypes and patient profiles. A total of 153 orthopedic procedures were initially registered in the study. There were 15 cancellations, and data were collected on 138 surgeries in 118 patients. The distribution of surgical subtypes is shown in Table I; 68% of all procedures involved the hip; the most common of these were joint replacements and decompression corings for avascular necrosis. The distribution of surgical subtypes varied among the four transfusion groups, but there was no significant difference in the distribution of surgical risk scores. Of the 15 surgeries that were cancelled, there were eight involving the hip, two tendon-lengthening procedures, and five other miscellaneous procedures. Cancellations were due to patient ineligibility, missing data, and cancelled procedures for medical indications.

Clinical and demographic characteristics of the patients are shown in Table II. There were 127 hemoglobin SS patients and eleven sickle β-thalassemia^0 patients. Fifty-five percent of all patients were female. The average age was 26 years old. Thirty-one percent of patients had a history of pulmonary disease: 83% of this group had previous acute chest syndrome, 7% had evidence of chronic lung disease, and 10% had other pulmonary diseases. Nineteen percent had a history of central nervous system (CNS) disease: 35% of these patients had a history of a cerebral vascular accident, 30% had cerebral palsy, 19% had isolated seizure disorders, and 16% had other CNS disease. The number of patients in each transfusion group is shown in Table II. There was no significant difference between the transfusion groups in demographic characteristics or baseline laboratory values except in the reported history of cardiac disease. Also, when second surgical procedures were eliminated, there was a difference in the transfusion history: 48% of the patients in group one had been transfused more than 10 times compared to 32% in group two, 24% in group three, and 62% in group four ($P = 0.02$).

Preoperative transfusion and perioperative management. The preoperative hemoglobin and hemoglobin

TABLE II. Laboratory and Clinical Characteristics of Orthopedic Patients (*N* = 138)[a]

Transfusion group	Group 1[b] (*N* = 34)		Group 2[b] (*N* = 40)		Group 3 (*N* = 24)		Group 4[b] (*N* = 40)		Total (*N* = 138)		
No. of patients	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%	p[a]
Sex											
Female	16	47%	24	60%	13	54%	23	58%	76	55%	ns
Male	18	53%	16	40%	11	46%	17	42%	62	45%	
Age											
<10 years	2	6%	3	8%	0	0%	3	8%	8	6%	ns
10–19 years	14	41%	16	40%	5	21%	16	40%	51	37%	
20+ years	18	53%	21	52%	19	79%	21	52%	79	57%	
Average age	24.4		24.6		28.6		27.3		26		
ASA											
2	13	38%	14	35%	11	46%	12	30%	50	36%	ns
3–4	21	62%	26	65%	13	54%	28	70%	88	65%	
Past medical history											
Pulmonary disease	12	35%	12	30%	5	21%	14	35%	43	31%	ns
Asthma	4	12%	5	13%	1	4%	4	10%	14	10%	ns
Smoking history	5	22%	3	10%	3	14%	8	26%	19	18%	ns
Cardiac disease	8	24%	2	5%	0		8	20%	18	13%	*
Renal disease	0		2	5%	2	8%	2	5%	6	4%	ns
CNS disease	9	26%	7	18%	2	8%	8	20%	26	19%	ns
#Hosp. in past year											ns
None	10	31%	6	16%	3	13%	8	22%	27	21%	
1–4	16	50%	25	68%	18	75%	22	61%	81	63%	
5+	6	19%	6	16%	3	13%	6	17%	21	16%	
Transfusion history											
Number of transfusions											
None	3	10%	1	3%	3	13%	2	5%	9	6%	ns
≤10	16	48%	24	60%	14	58%	15	38%	69	51%	
>10 prior transfusions	14	42%	15	37%	7	29%	22	56%	58	43%	
Prior alloimmunization	10	29%	7	18%	9	39%	9	23%	35	26%	ns
Previous Tx reaction	5	15%	7	18%	2	8%	2	5%	16	12%	ns
Preop. labs											
Preop Hypoxia	0		0		0		2	10%	2	2%	ns
Abnormal CXR	4	13%	4	13%	4	27%	6	21%	18	17%	ns
Abnormal LFT	2	7%	2	7%	1	6%	4	12%	9	8%	ns
Abnormal creatinine	2	7%	0		0		0		2	2%	ns
Mean baseline Hb	8.8		8.4		9.2		8.8		8.7		ns
Mean preop Hb	10.9		10.6		9		10.3		10.3		**
Mean preop S%	38%		58%		89%		25%		49%		***
Surgical risk score											
Risk = 1	15	44%	22	55%	17	71%	26	65%	80	58%	ns
Risk = 2	19	56%	18	45%	7	29%	14	35%	58	42%	

[a]The comparison of the distributions of clinical characteristics across the 4 groups were made using chi-squre analysis for categorical data and ANOVA for the continuous variables. Significant differences are noted as follows: $*P \leq 0.05$; $**P \leq 0.001$; $***P \leq 0.0001$.
[b]There are no differences in the clinical characteristics between the randomized arms except in the incidence of cardiac disease ($P \leq 0.05$).

S for the population as a whole were 10.3 ± 1.7 g/dl and 49% ± 25%, respectively. Group three had a significantly lower preoperative hemoglobin than the other groups: 9.0 g/dl in group three, compared to 10.9 g/dl in group one, 10.6 g/dl in group two, and 10.3 g/dl in group four, $P = 0.0002$. The preoperative hemoglobin S % was also significantly different across the groups: 38% in group one; 58% in group two; 89% in group three; and 25% in group four ($P = 0.0001$). As expected, the preoperative hemoglobin did not differ between the randomized groups but the preoperative percent of hemoglobin S varied significantly ($P = 0.0001$). Of note, 73% of the patients in group one underwent exchange transfusion, compared to 10% in group two.

Seventy-nine percent of the patients received preoperative hydration, and over 97% were extensively monitored intraoperatively, including measurements of cardiac rhythm (ECG), blood pressure, temperature, and oxygen saturation. Active intraoperative warming (defined as the use of one or more of the following methods of temperature conservation: warming blanket, humidifier, blood/fluid warmer, heat lamp, or ambient room

TABLE III. Complications in 138 Orthopedic Procedures*

Any Perioperative Complications[a]	Total group ($N = 138$)	%	Hip replacement ($N = 52$)	%	Hip coring ($N = 22$)	%
Intraoperative/PACU	73	53%	48	92%	5	23%
Excessive blood loss (>10% EBL)	61	44%	37	71%	2	9%
Other	27	20%	11	21%	4	18%
Acute chest syndrome (ACS)	16	12%	8	15%	3	14%
Miscellaneous postoperative	18	13%	12	23%	1	5%
Fever/infection	19	14%	8	15%	1	5%
Vaso-occlusive episode (VOE)	13	9%	6	12%	2	9%
Neurologic	5	4%	2	4%	1	5%
Renal	1	1%	1	2%	0	0%
Death	2	1%	1	2%	0	0%
Sickle-cell event (ACS/VOE)	23	17%	10	19%	4	18%
Any serious complication	92	67%	50	96%	10	45%

*Complications associated with transfusions are excluded here. Percentages are the proportion of operations in each group associated with a complication.
[a]Includes preoperative period after transfusion.

temperature) was provided in 74% of cases. Length of anesthesia and type of surgery did not predict the use of active temperature conservation. There was no difference in the intraoperative management or the distribution of anesthetic regimens across the groups: 80% of the cases received general anesthesia. Furthermore, there was also no difference in the anesthesia time and postoperative pain control techniques across the transfusion groups. Postoperatively, 99% of the patients were hydrated intravenously, 93% received supplemental oxygen, 85% were treated with antibiotics, and 37% received chest physiotherapy and incentive spirometry.

Complications. Only serious or life-threatening complications were analyzed in detail and are summarized in Table III. The most common of these were intraoperative complications, which occurred in one-half of the procedures: the majority of these intraoperative events were excessive blood loss. Hypothermia was the next most common intraoperative complication, which occurred in 15 cases (11%). Whether a patient was actively warmed did not predict the development of intraoperative hypothermia (temperature < 35.5°C). Sickle cell-related events (acute chest syndrome and/or vaso-occlusive crisis) were associated with 17% of the procedures. Specific and overall complication rates did not differ significantly between the randomized transfusion groups. There were no significant differences in complication rates across all four transfusion groups except in the occurrence of acute chest syndrome: 21% in group one; 8% in group two; 21% in group three; and 3% in group four ($P = 0.04$).

Surgical risk score was the only preoperative predictor of postoperative complications: 93% of patients in the higher surgical risk category developed a serious complication compared to only 48% in the low risk group ($P = 0.001$). Higher risk procedures were more likely to be associated with excessive intraoperative blood loss (84% vs 99%, $P = 0.001$), and intraoperative blood loss was also associated with a higher postoperative complication rate (48% vs 25%, $P = 0.038$). Of note, intraoperative hypothermia was associated with a higher overall postoperative complication rate, but this difference was not statistically significant. We were unable to identify any statistically significant predictor of sickle cell-related perioperative complications.

Twelve percent of the patients had a transfusion-related complication. New antibody formation was the most common of these complications and occurred in 9% of the patients. Delayed hemolytic reactions were documented in 5 patients. Transfusion-related complications were more common in the aggressive transfusion group than in the conservative group, but the difference was not statistically significant (24% vs 15%, $P = 0.52$).

There were two deaths in the study. The first patient was a 43-year-old man in group one who underwent revision of a right hip arthroplasty. This patient had avascular necrosis of both hips, for which he had undergone hip replacements, and he had a history of right-sided heart failure and recurrent acute chest syndrome. During surgery, he required 10 units of packed red blood cells, 8 units of fresh frozen plasma, cryoprecipitate, and platelets. He developed acute chest syndrome and required multiple postoperative transfusions and another surgical procedure for evacuation and drainage of an incisional hematoma. Despite aggressive treatment, the patient developed multiorgan failure and expired on postoperative day 24.

The other death occurred in a 16-year-old man entered in the non-transfusion group. His past medical history was notable for recurrent acute chest syndrome, splenectomy, cholecystectomy, and recurrent painful episodes. He was admitted for fever and extremity pain. After developing joint swelling, he underwent drainage and biopsy of the left elbow. He defervesced and was treated for 13 days with antibiotics for a diagnosis of osteomy-

elitis. At day 15, he developed acute chest syndrome. Despite aggressive treatment, he died of respiratory failure. The autopsy confirmed bronchopneumonia with a large right ventricular outlet thrombosis.

Hip Replacement and Coring Procedures

Hip replacement. There were 52 hip replacement surgeries in 45 patients: seven patients had two separate operations. The average age of the patients was 33.9 ± 13.8 years. Seventy-four percent were total hip replacements, 14% were hemiarthroplasties, and 12% were revisions. Advanced symptomatic avascular necrosis was the indication for surgery in all but three of the cases, in which the preoperative diagnosis was rheumatoid arthritis. Fifty-three percent of the patients had a history of bilateral arthritis. Seventy-three percent of these procedures were performed under general anesthesia, and 27% were performed under regional anesthesia alone. Average anesthesia time was 4.5 ± 1.5 h.

The complication rates associated with total hip replacements are shown in Table III. The average blood loss was 1204 ± 1079 ml (median of 800 and range 100–6000 ml). Sixty-two percent of patients required intraoperative transfusions, and an additional 33% required postoperative transfusions. Male patients had significantly more blood loss then females (1433 ± 1167 cc versus 1037 ± 996 cc, $P \leq 0.01$). Duration of anesthesia and patient age were also correlated with intraoperative blood loss ($R = 0.41$, $P = 0.003$ and $R = 0.31$, $P = 0.03$, respectively). There was no significant relationship between intraoperative blood loss and preoperative transfusion group, patient weight, surgical approach, or the use of intraoperative epidural anesthesia.

Acute chest syndrome or vaso-occlusive crisis occurred after 19% of hip replacements, and fever or infection was seen after 15%. Postoperative surgical complications were reported in eight (15%) of the procedures, including immediate postoperative hemorrhage, wound hematomas requiring evacuation, dislocated prostheses, wound infection with abscess, and rupture of the femoral prosthesis through the acetabulum. There were no significant differences in the complication rates between the two randomized transfusion groups. Since only 12% of the patients were enrolled in the non-transfusion group, a statistical comparison of the complication rates in this group to the transfused groups was not performed. The mean hospitalization time was 18.5 ± 20.3 days with a median of 12.5 days.

Hip coring. There were 22 hip coring procedures in 21 patients. The average age of the patients undergoing hip coring procedures was 25 ± 8.5 years. Eleven (50%) were enrolled in the non-transfusion group. All patients were diagnosed with symptomatic avascular necrosis, and bilateral disease was documented in 64% of the patients. Eight (36.4%) of the procedures were performed on the right hip, eight (36.4%) on the left, and six (27.2%) on both hips simultaneously (total of 28 hips). Eighty-one percent of these joints had Ficat stage I or II disease, and 19% had stage III disease. The mean duration of anesthesia was 2.5 ± 1.1 h; 82% of patients underwent general anesthesia, and 18% had regional anesthesia alone. Complication rates are shown in Table III. Intraoperative or PACU complications occurred in five patients (23%) and included significant blood loss in one patient, hypothermia in three patients, and transient drop in oxygen desaturation in one. Acute chest syndrome was documented in three (14%) patients, all of whom were registered in the non-transfusion group. Only one surgical complication was recorded: infection at the incision site requiring 3 days of intravenous antibiotics. The average hospital stay was 9.5 ± 9.0, and the median was 5.5 days.

Comparison of hip replacement and hip coring. The patients undergoing hip coring were significantly younger than those undergoing hip replacement procedures and were more likely to have been enrolled in the non-transfusion group. However, there were no other significant differences in the demographic characteristics of the two groups. There was no difference in the preoperative hemoglobin levels, but there was a significantly lower mean preoperative hemoglobin S percentage in the patients undergoing hip replacement (46% vs 72%, $P = 0.0009$). Although the rate of sickle cell complications was the same, the overall complication and intraoperative complication rates were lower in the hip coring group. The duration of anesthesia, days until postoperative ambulation, and duration of hospitalization were also significantly lower in the hip coring patients.

DISCUSSION

As patients with sickle cell anemia live longer, the majority of adults will require orthopedic surgical intervention. The purpose of this study was to define the perioperative risk in patients receiving standardized multidisciplinary care. This report of 138 surgeries, which were followed prospectively, is the largest collection of orthopedic surgeries in sickle cell disease. We demonstrate a substantially higher rate of perioperative complications than reported in general orthopedic populations [15,17–20]. Specifically, over two-thirds of the orthopedic patients in the study had a serious complication, and 17% developed acute chest syndrome or vaso-occlusive episodes. In the 54% of these patients randomized to a preoperative transfusion regimen, we found no advantage to aggressive preoperative transfusion when compared to a simple preoperative transfusion regimen in the prevention of these complications. In addition, we found that, when compared to hip replacement surgery, hip coring for avascular necrosis of the hip was associated with

fewer complications and required less hospitalization time.

The perioperative complication rates did not differ between the conservative and aggressive transfusion groups [14,21]. This finding supports a growing body of clinical and in vitro evidence that suggests that limited dilution of sickle cells and partial correction of the anemia are beneficial [3,5,13,32,37,40,43,49,56]. Specifically, it appears that a hemoglobin S level of 50–60% is clinically equivalent to 30%. The safety of no preoperative transfusion in orthopedic surgery could not be answered by this study: there were only a small number of patients in the non-transfusion group, and they were not randomly assigned. Preoperative transfusion in sickle cell disease is generally recommended to improve the oxygen-carrying capacity and rheologic characteristics of the red cells. However, the frequency of transfusion reactions in patients with sickle cell disease is higher than in other patients undergoing surgery [16,30]. The finding that 21% of aggressively transfused patients (group one) and 9% of the total study group developed a new alloantibody underlines the recent recommendations for the use of phenotypically matched blood for all sickle cell patients in the perioperative period [16,30,31]. New studies support the use of phenotypically matched blood for sickle cell disease patients, because it is cost-effective and eliminates the problem of transfusion reactions [16,31].

Acute chest syndrome occurred in 15% of the procedures and was the primary factor in the two deaths in this study. In patients who do not have sickle cell anemia, the frequency of pulmonary complications range from 1% to 70% [32–39]. Most of these events were minor and thought to be attributable to atelectasis, which was excluded from this analysis. The etiology of acute chest syndrome is multifactorial and includes infection, pulmonary infarction and pulmonary fat embolism [40]. Specifically, since the rate of pulmonary fat embolism in bone injuries and orthopedic procedures is high, the sickle cell population may be at particular risk for this event in the perioperative period of orthopedic surgery [41,42].

The overall complication rate from total hip replacements in our population of sickle cell patients was significantly higher than in non-sickle cell patients, a finding supported by previous reports [43–50]. The blood loss associated with this procedure is a particular concern in this population with prior exposure to blood products and high alloimmunization rates. The mean blood loss of 1,204 cc is at the high end of blood loss associated with hip replacement in non-sickle cell patients (ranges from 180 to 1400 cc) [51–59]. As expected from previous studies, intraoperative blood loss was associated with anesthesia time, which is almost twice as long in sickle cell patients than in non-sickle cell patients [52,54]. Similar to control populations, gender and age were also correlated to blood loss [45,53,58].

Complications associated with hip replacement and necessary preoperative preparation resulted in a mean hospitalization time of nineteen days. In contrast, a stay of approximately 12 days has been reported in the general population [58]. The mortality rate in this study was 1.9% and like morbidity, was secondary to pulmonary complications. Seagrott et al. reported a mortality rate of 11 per 1,000 operations (1.1%) in 11,607 total hip replacements in the general population [59]. In non-sickle cell patients, cardiovascular and thromboembolic disease, not pulmonary complications, was the main cause of death.

In contrast to hip replacement, the perioperative morbidity of decompression coring reported in previous studies is acceptable [60,61]. Although the patients undergoing hip coring were younger, we were unable to demonstrate any other significant differences in their demographic characteristics. However, we cannot rule out selection bias as a larger percentage of patients undergoing hip coring were enrolled in the non-transfusion group. The complication rates (following hip coring decompression) in this series were higher than in non-sickle cell populations and resulted in a longer mean hospital stay compared to other study groups. This was most likely due to sickle cell-related events. For example, serious pulmonary events in large series of decompression coring studies are rare: Steinberg found one event in 200 cases [62]. In contrast, acute chest syndrome and painful events accounted for more than half of the postoperative complications in our patients. All acute chest syndrome events occurred in the non-transfusion patients, which supports our previous observations about the benefit of transfusion therapy in preventing pulmonary disease [21,63]. However, the small number of non-transfused patients in this study and the possibility of selection bias seriously limit the interpretation of these results. As our study only followed patients through a 30-day postoperative period, a prospective trial is needed to evaluate both the short and long-term benefits of hip-coring decompression in sickle cell anemia.

In summary, this report provides information for physicians to share with the growing number of sickle cell patients with orthopedic disease about the risks of surgery. This study supports the results previously published by the National Preoperative Transfusion in Sickle Cell Disease Group. These results stated that a conservative preoperative transfusion regimen to bring hemoglobin concentration to between 9 and 11 g/dl was as effective as an aggressive transfusion regimen in which the hemoglobin S level was lowered to 30%. This study also lays the foundation for a randomized prospective trial to determine the perioperative and long-term efficacy of core

decompression for avascular necrosis of the hip in sickle cell disease.

APPENDIX

Participating Investigators (Preoperative Transfusion in Sickle Cell Disease Study Group) and Number of Patients Enrolled in the Study from Each Institution

R. Nagel, Albert Einstein College of Medicine (Bronx, NY) (1); R. Johnson, Alta Bates Hospital (Berkeley, CA); D. Sears, Baylor College of Medicine (Houston, TX); M. Wong, Bronx-Lebanon Hospital (Bronx, NY); J. Parke, Carolinas Medical Center (Charlotte, NC); G. Bray, Children's Hospital National Medical Center (Washington, DC) (2); D. Hurst, L. Koblenz, and E. Vichinsky, Children's Hospital Oakland (Oakland, CA) (10); P. DeAlarcon and M. Grossi, Children's Hospital of Buffalo (Buffalo, NY); K. Ohene-Frempong, Children's Hospital of Philadelphia (Philadelphia, PA) (10); P. Waldron and M. Walters, Children's Hospital, Seattle (Seattle, WA) (1); C. Russo, S. Murphy, and H. Smith, Children's Memorial Hospital (Chicago, IL); G. Woods, Children's Mercy Hospital (Kansas City, MO) (1); L. Guarini, A. Hurlet, and S. Piomelli, Columbia-Presbyterian Medical Center (New York, NY) (5); T. Kinney, and G. Phillips, Duke University Medical Center (Durham, NC) (9); C. Daeschner, and T. Holbrook, East Carolina University (Greenville, NC) (2); I. Buchanan, and J. Eckman, Emory University (Atlanta, GA) (2); S. Claster, Highland Hospital (Oakland, CA); H. Hume, Hospital Ste-Justine (Montreal, Quebec, Canada) (1); N. Oliveri, Hospital for Sick Children (Toronto, Ontario, Canada) (1); R. Bellevue, Interfaith Medical Center (Brooklyn, NY) (5); V. Mankad and W. Wang, Le Bonheur Children's Medical Center (Memphis, TN); P. Milner, Medical College of Georgia (Augusta, GA) (6); M. Abboud, and S. Jackson, Medical University of South Carolina (Charleston, SC) (2); L. Benjamin, M. Bestak, and E. Radel, Montefiore Hospital (Bronx, NY) (1); S. Baruchel and D. Essentine, Montreal Children's Hospital (Montreal, Quebec, Canada); F. Blei, New York University Medical Center (New York, NY); S. Embury, and W. Mentzer, San Francisco General Hospital (San Francisco, CA) (2); P. Gillette, S. Miller, and S. Rao, State University of New York (Brooklyn, NY) (2); R. Grover, G. Ramirez, and D. Wethers, St. Luke's/Roosevelt Hospital (New York, NY) (4); B. Glader and C. Russo, Stanford University Children's Hospital (Stanford, CA); W. Jennings, Truman Medical Center (Kansas City, MO); D. Rucknagel and K. Kalinyak, University of Cincinnatti (Cincinnatti, OH) (1); P. Lane, University of Colorado (Denver, CO); M. Koshy, and N. Talischy, University of Illinois (Chicago, IL) (25); C. Pegelow, University of Miami (Miami, FL) (17); R. Iyer, and M. Steinberg, University of Mississippi (Jackson, MS) (4); H. Cooper, and E. Orringer, University of North Carolina (Chapel Hill, NC) (11); V. Mankad and Y. Yang, University of South Alabama (Mobile, AL) (2); C. Johnson, and D. Powars, USC Medical Center (Los Angeles, CA) (11).

ACKNOWLEDGMENTS

The authors acknowledge Shanda Robertson for her data management and Karen Seth for her editorial support.

REFERENCES

1. Epps CH Jr, Bryant DD, 3rd, Coles MJ, Castro O. Osteomyelitis in patients who have sickle cell disease. J Bone Joint Surg (Am) 1991; 73:1281–1294.
2. Hopson C, Siverhus S. Ischemic necrosis of the femoral head. J Bone Joint Surg 1988;70:1048–1051.
3. Al-Jam'a AH, Al-Dabbous IA, Abdalla E, Al-Jishi N. Avascular necrosis of the femoral and humeral heads in sickle cell disease: Experience at Qatif Central Hospital, Saudi Arabia. Saudi Med J 1995;16: 252–256.
4. Chung S, Ralston E. Necrosis of the femoral head associated with sickle cell anemia and its genetic variants. J Bone Joint Surg 1969; 51:33–58.
5. Milner PF, Kraus AP, Sebes JI, Sleeper LA, Dukes KA, Embury SH, Bellevue R, Koshy M, Moohr JW, Smith J. Sickle Cell disease as a cause of osteonecrosis of the femoral head. N Engl J Med 1991;325: 1476–1481.
6. Styles LA, Vichinsky EP. Core Decompression in avascular necrosis of the hip in sickle cell disease. Am J Hematol 1996;52:103–107.
7. Bentley PG, Howard ER. Surgery in children with homozygous sickle cell anemia. Ann R Coll Surg Engl 1979;66:55.
8. Griffin TC, Buchanan GR. Elective surgery in children with sickle cell disease without preoperative blood transfusion. J Pediatr Surg 1993; 28:681–685.
9. Gross ML, Schwedler M, Bischoff RJ, Kerstein MD. Impact of anesthetic agents on patients with sickle cell disease. Am Surgeon 1993; 59:261–264.
10. Janik J, Seeler RA. Perioperative management of children with sickle hemoglobinopathy. J Pediatr Surg 1980;15:117–120.
11. Koshy M, Weiner J, Miller S, Sleeper L, Vichinsky E, Brown A, Khakoo Y, Kinney T, The cooperative study of sickle cell disease: surgery and anesthesia in sickle cell disease. Blood 1995;86:3676–3686.
12. Morrison JC, Whybrew WD, Bucovaz ET. Use of partial exchange transfusion preoperatively in patients with sickle cell hemoglobinopathies. Am J Obstet Gynecol 1978;132:59–63.
13. Ware R, Filston HC, Schultz WH, Kinney TR. Elective cholecystectomy in children with sickle hemoglobinopathies: successful outcome using a preoperative transfusion regimen. Ann Surg 1988;208:17–35.
14. Vichinsky E, Haberkern C, Neumayr L, Earles A, Black D, Koshy M, Pegelow C, Abboud M, Ohene-Frempong K, Iyer R. The preoperative transfusion in sickle cell disease study group. A comparison of conservative and aggressive transfusion regimens in the perioperative management of sickle cell disease. N Engl J Med 1995;333:206–213.
15. Cohen MM, Duncan PG: Physical status score and trends in anesthetic complications. J Clin Epidemiol 1988;41:83–90.

16. Pretransfusion testing. In:Walker RH, editor. Technical Manual, 10th edition. Arlington: American Association of Blood Banks; 1990.
17. Cohen MM, Duncan PG, Tate RB. Does anesthesia contribute to operative mortality? J Am Med Assoc 1988;260:2859–2863.
18. Derrington MC, Smith G. A review of studies of anaesthetic risk, morbidity and mortality. Br J Anaesth 1987;59:815–833.
19. Katzner M, Babin S, Schvingt E. Complications observed in a series of 2018 total hip replacements. Nouv Presse Med 1982;11:181–183.
20. Noer HH, Jensen LP, Gottlieb J, Mortensen JS, Kalms SB, Jorgensen S, Torholm C. Data registration of postoperative complications in connection with orthopedic surgery. Ugeskr Laeger 1991;153:1587–1590.
21. Haberkern CM, Neumayr LD, Orringer EP, Earles AN, Robertson SM, Black D, Abboud MR, Koshy M, Idowu O, Vichinsky EP. The preoperative transfusion in sickle cell disease study group. Cholecystectomy in sickle cell anemia patients: perioperative outcome of 364 cases from the national preoperative transfusion study. Blood 1997;89:1533–1542.
22. Cohen AR, Martin MB, Silber JH, Haewon KC, Ohene-Frempong K, Schwartz E. A modified transfusion program for prevention of stroke in sickle cell disease. Blood 1992;9:1657–1661.
23. Bischcoff RJ, Williams A, Dalali MJ, Rice JC, Kerstein MD. Assessment of the use of transfusion therapy perioperatively in patients with sickle cell hemoglobinopathies. Ann Surg 1988;207:434–438.
24. Cohen AR, Martin MB, Silber JH, Haewon KC, Ohene-Frempong K, Schwartz E. A modified transfusion program for prevention of stroke in sickle cell disease. Blood 1992;9:1657–1661.
25. Jan KM, Usami S, Smith JA. Effects of Transfusion on rheological properties of blood in sickle cell anemia. Transfusion 1982;22:17–20.
26. Lessin LS, Kurantsin-Mills J, Klug PP, Weems HB. Determination of rheologically optimal mixtures of Aa and Ss erythrocytes for transfusion. Prog Clin Biol Res 1978;20:124–134.
27. Miller ST, Jensen D, Rao SP. Less intensive long-term transfusion therapy for sickle cell anemia and cerebrovascular accident. J Pediatr 1992;120:54–57.
28. Murphy JR, Wengard M, Brereton W. Rheological Studies of Hb Ss Blood: Influence of hematocrit, hypertonicity, separation of cells, deoxygenation, and mixture with normal cells. J Lab Clin Med 1976;87:475–486.
29. Schmalzer EA, Lee JO, Brown AK, Usami S, Chien S. Viscosity of mixtures of sickle and normal red cells at varying hematocrit levels: Implications for transfusion. Transfusion 1987;27:228–233.
30. Vichinsky EP. Transfusion therapy. In: Embury SH, Hebbel RP, Mohandas N, Steinberg MH, editors. Sickle cell disease: Basic principles and clinical practice. New York: Raven Press; 1994. p 781–798,
31. Tahhan HR, Holbrook CT, Braddy LR, Brewer LD, Christie JD. Antigen-matched donor blood in the transfusion management of patients with sickle cell disease. Transfusion 1994;34:562–569.
32. Celli BR, Rodriguez KS, Snider GL. A Controlled trial of intermittent positive pressure breathing, incentive spirometry, and deep breathing exercises in preventing pulmonary complications after abdominal surgery. Am Rev Respir Dis 1984;130:12–15.
33. Engberg G, Wiklund L. Pulmonary complications after upper abdominal surgery: their prevention with intercostal blocks. Acta Anaesthesiol Scand 1988;32:1–9.
34. Jayr C, Mollie A, Bourgain JL, Alarcon J, Masselot J, Lasser P, Denjean A, Truffa-Bachi J, Henry-Amar M. Postoperative pulmonary complications: general anesthesia with postoperative parenteral morphine compared with epidural analgesia. Surgery 1988;104:57–63.
35. Pflug AE, Murphy TM, Butler SH, Tucker GT. The effects of postoperative peridural analgesia on pulmonary therapy and pulmonary complications. Anesthesiology 1974;41:8–17.
36. Roukema JA, Carol EJ, Prins JG. The prevention of pulmonary complications after upper abdominal surgery in patients with noncompromised pulmonary status. Arch Surg 1988;123:30–34.
37. Spence AA, Smith G. Postoperative Analgesia and Lung Function: A comparison of morphine with extradural block. Br J Anaesthiol 1971;43:144–148.
38. Strandberg A, Tokics L, Brismar B, et al. Atelectasis during anaesthesia and in the postoperative period. Acta Anaesthesiol Scand 1986;30:154–158.
39. Vodinh J, Bonnet F, Touboul C, et al. Risk factors of postoperative pulmonary complications after vascular surgery. Surgery 1989;105:360–365.
40. Vichinsky E, Williams R, Das M, Earles AN, Lewis N, Adler A, McQuitty J. Pulmonary fat embolism: a distinct cause of severe acute chest syndrome in sickle cell anemia. Blood 1994;83:3107–3112.
41. Fabian TC, Hoots AV, Stanford DS, Patterson CR, Mangiante EC. Fat embolism syndrome: prospective evaluation in 92 fracture patients. Crit Care Med 1990;18:42–46.
42. Maxeiner H. Significance of pulmonary fat embolism in intra- and early postoperative fatal cases following femoral fractures of the hip region. Orthopade 1995;24:94–103.
43. Acurio MT, Friedman RJ. Hip Arthroplasty in patients with sickle cell haemoglobinopathy. J Bone Joint Surg (Br) 1992;74:367–371.
44. Bishop A, Roberson J, Eckman J, Fleming L. Total hip arthroplasty in patients who have sickle cell hemoglobinopathy. J Bone Joint Surg (Am) 1988;70:853–855.
45. Clarke HJ, Jinnah RH, Brooker AF, Michaelson JD. Total replacement of the hip for avascular necrosis in sickle cell disease. J Bone Joint Surg 1989;71-B:465–470.
46. Gunderson C, D'Ambrosia RD, Shoji H. Total hip replacement in patients with sickle cell disease. J Bone Joint Surg (Am) 1977;59:760–762.
47. Hanker G, Amstutz H. Osteonecrosis of the hip in the sickle cell diseases: treatment and complications. J Bone Joint Surg (Am) 1988;70:499–506.
48. Hickman JM, Lachiewicz PF. Results and complications of total hip arthroplasties in patients with sickle cell hemoglobinopathies: role of cementless components. J Arthroplasty 1997;12:420–425.
49. Moran M, Huo M, Garvin K, Pellicci P, Salvati E. Total hip arthroplasty in sickle cell hemoglobinopathy. Clin Orthop 1993;294:140–148.
50. Sanjay BK, Moreau PG. Bipolar hip replacement in sickle cell disease. Int Orthop 1996;20:222–226.
51. Biesma DH, Van Iperen CE, Kraaijenhagen RJ, Marx JJ, Van De Wiel HB, Van De Wiel A. Red blood cell transfusions for total hip replacement in a regional hospital. Vox Sang 1994;66:270–275.
52. Flordal PA, Neander G. Blood loss in total hip replacement. Arch Orthop Trauma Surg 1991;111:34–38.
53. Grosflam JM, Wright EA, Cleary PD, Katz JN. Predictors of blood loss during total hip replacement surgery. Arthritis Care Res 1995;8:167–173.
54. Maruyama M, Takei H, Takei T, Kitagawa E. The factors that influence intraoperative blood loss during total hip replacement. Masui 1992;41:1180–1182.
55. Robinson CM, Christie J, Malcolm-Smith N. Nonsteroidal antiinflammatory drugs, perioperative blood loss, and transfusion requirements in elective hip arthroplasty. J Arthroplasty 1993;8:607–610.
56. Schneeberger AG, Schulz RF, Ganz R. Blood loss in total hip arthroplasty. Arch Orthop Trauma Surg 1998;117:47–49.
57. Sharrock NE, Mineo R Urquhart B, Salvati EA. The effect of two levels of hypotension on intraoperative blood loss during total hip arthroplasty performed under lumbar epidural anesthesia. Anesth Analg 1993;76:580–584.
58. Boettcher WG. Total hip arthroplasties in the elderly. Clin Orthop 1992;274:30–34.

59. Seagroatt V, Tan HS, Goldacre M, Bulstrode C, Nugent I, Gill L. Elective total hip replacement: incidence, emergency readmission rate, and postoperative mortality. Br Med J 1991;303:1431–1435.
60. Fairbank AC, Bhatia D, Jinnah RJ, Hungerford DS. Long-term results of core decompression for ischaemic necrosis of the femoral head. J Bone Joint Surg (Br) 1995;77:42–49.
61. Steinberg ME, Brighton CT, Corces A, Hayken GD, Steinberg DR, Strafford B, Tooze SE, Fallon M. Osteonecrosis of the femoral head: results of core decompression and grafting with and without electrical stimulation. Clin Orthop 1989;249:199–207.
62. Steinberg ME. Core decompression of the femoral head for avascular necrosis: indications and results. Can J Surg 1995;38(Suppl 1):S18–S24.
63. Vichinsky E, Styles L. Pulmonary complications. Hematol Oncol Clin North Am 1996;10:1275–1287.